UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,054	11/01/2000	Robert D'Amato	9516-0039-999	3798

20583 7590 03/09/2010

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
03/09/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/704,054	D'AMATO, ROBERT	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,29,73,76 and 77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,29,73,76 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/3/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 2/3/2010, are acknowledged and entered. Claim 77 is newly added. Claims 23, 29, 73, and 76-77 are pending and under examination.

Response to Arguments

Applicants' arguments, filed 2/3/2010, have been fully considered and are persuasive. Specifically, amendments to claims 23 and 73 exclude the patient population taught in the cited prior art. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 2/3/2010. The Examiner has considered the references cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 – 1st Paragraph - New Ground of Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23, 29, 73, and 76-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of

Patent Applications Under the 35 U.S.C. 112, 1st "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. **This is a New Matter rejection**.

The claims are drawn to methods of treating a blood-born tumor (claims 23 and 77) or leukemia (claim 73) comprising administration of thalidomide, wherein the patient is "not a leukemia patient who has graft-versus-host disease" or "wherein said patient does not have graft-versus-host disease". The amended claims thus exclude particular patients, *i.e.*, patients having a blood-born tumor (*e.g.*, leukemia) but who do not have graft-versus-host disease. There is no basis in the originally filed disclosure for the specific exclusion of such patients from the claimed treatment methods.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

Applicant relies on the originally filed specification at page 5, lines 12-19, page 8, lines 3-12, page 9, lines 7-9, and page 20, lines 20-24 as providing support for exclusion of patients having blood-born tumors but who do not have graft-versus-host disease. The cited sections of the originally filed specification are reproduced below for ease of discussion.

> "...retinoblastoma, Ewing sarcoma, neuroblastoma, and osteosarcoma. A tumor cannot expand without a blood supply to provide nutrients and remove cellular wastes. Tumors in which angiogenesis is important include solid tumors, and benign tumors such as acoustic neuroma, neurofibroma, trachoma and pyogenic granulomas. Prevention of angiogenesis could halt the growth of these tumors and the resultant damage to the animal due to the presence of the tumor" --- **page 5, lines 12-19 of originally filed specification**

> "Thus, a method and composition are needed that are capable of inhibiting angiogenesis and which are easily administered. A simple and efficacious method of treatment would be through the oral route. If an angiogenic inhibitor could be given by an oral route, the many kinds of diseases discussed above, and other angiogenic dependent pathologies, could be treated easily. The optimal dosage could be distributed in a form that the patient could self-administer" --- **page 8, lines 3-12 of originally filed specification**

> "It is another object of the present invention to provide a treatment for diseases mediated by angiogenesis" --- **page 9, lines 7-9 of originally filed specification**

> "...e.g. Shealy et al., Chem. Indus. 1030 (1965); and Casini et al., Farmaco Ed. Sci. 19:563 (1964). The compounds described above can be provided as pharmaceutically acceptable formulations using formulation methods known to those of ordinary skill in the art." --- **page 20, lines 20-24 of originally filed specification**

None of the cited sections of the originally filed specification provide support for exclusion of patients having a blood-born tumor but who do not have graft-versus-host disease.

Applicant further cites column 12, lines 10-12 of U.S. Patent No. 5,629,327[1] as providing support exclusion of the recited patient population. In context, the cited section of USP No. 5,629,327 states, "The epoxide containing angiogenesis inhibitors, with or without epoxide hydrolase inhibitors, are also effective in treating diseases such as septic shock, leprosy and graft vs. host disease". This same language is found in the instant specification at page 19, lines 12-15. Nowhere does the cited section suggest that Applicant contemplated treating patients having a blood-born tumor but who did not have graft-versus-host disease as recited in the amended claims.

Accordingly, exclusion of patients having a blood-born tumor but who do not have graft-versus-host disease is not supported by the originally filed disclosure.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103 – New Ground of Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23, 29, and 76-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Olson *et al.*** (Clinical Pharmacology and Therapeutics, 1965, vol. 6, no. 3, pages 292-297).

---

[1] The instant application claims priority to U.S. Non-Provisional Application No. 08/168,817, which issued as U.S. Patent No. 5,629,327.

The instant claims recite methods of treating a blood-born tumor (e.g., leukemia) comprising orally administering between approximately 0.5 and approximately 50 mg/kg/day thalidomide in a capsule.

Olson *et al.* disclose oral administration of thalidomide to patients with advanced malignancy who had a relapse of failed to respond to usual chemotherapy (page 293, left column, "Method of study"). Thalidomide was initially given in a dose of 200 mg orally three times per day, which for an average human weighing 70 kg is approximately 8.6 mg/kg/day (*id.*).

Regarding treatment of patients with blood-born tumors, two of the treated patients had multiple myeloma, which is a blood-borne tumor as recited in the instant claims.

While no objective responses were observed in the treated patients, Olson *et al.* disclose that in one patient with multiple myeloma "the rapid progression of the disease appeared to be slowed" (paragraph bridging pages 294 and 295). Both multiple myeloma patients also showed "subjective improvement" (Table I). Accordingly, it is clear that thalidomide was effective to "treat" patients having multiple myeloma by slowing disease progression and providing subjective improvement to the treated patients.

Olson *et al.* suggest and motivate further studies of thalidomide in treating tumors. In this regard, the authors state that there may be periods in the development of tumors when sensitivity to thalidomide may be present and the absence of serious hematologic and other systemic toxicity and the "substantial subjective palliation" obtained from thalidomide therapy combine to make this drug "suitable for full-scale Phase II trial in patients with tumors resistant to all known present agents" (page 296, right column). The authors conclude that "[I]t is suggested that further trial of this drug in tumors not sensitive to other agents, especially tumors of mesenchymal origin, and its use in conjunction with x-ray therapy, is warranted" (page 297, left column).

It would have been *prima facie* obvious to orally administer thalidomide in a capsule to patients having multiple myeloma in a Phase II clinical trial to evaluate the clinical activity of this drug at the time the invention was made. The skilled artisan would have been motivated to do so because oral administration of thalidomide to patients having multiple myeloma has been demonstrated to slow disease progression and to provide subjective improvement to such patients. While no objective responses were observed by Olson *et al.*, the authors admit that

their studies were not an adequate drug trial and the data cannot serve to indicate lack of activity of thalidomide against tumors in man (page 296, paragraph bridging left and right columns). In light of the slowing of disease progression and subjective improvement observed in multiple myeloma patients treated with thalidomide, the skilled artisan would have been motivated to test thalidomide in a proper Phase II clinical trial as explicitly suggested and motivated by Olson *et al*. The skilled artisan would have been imbued with at least a reasonable expectation that thalidomide would be effective to "treat" patients with multiple myeloma by slowing disease progression and providing subjective improvement to the treated patients as evidence by Olson *et al*.

Regarding providing thalidomide in a capsule, while Olson *et al*. do not explicitly disclose in what form thalidomide was orally administered, capsules are a well-known and common means to provide therapeutic agents for oral administration. As such, providing thalidomide in a capsule for oral administration would have been obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23, 29, 73, and 76-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 6 of U.S. Patent No. 7,435,745. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treating "blood-borne tumors" comprising administering thalidomide in combination with dexamethasone as recited in the '745 patent claims anticipates the claimed method of treating "blood-born tumors" comprising administering thalidomide". The "comprising" language of the instant claims allows for the administration of other active agents such as dexamethasone as recited in the claims of the '745 patent.

Claims 23, 29, 73, and 76-77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-30 of copending Application No. 12/249,847. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treating "blood-born cancer" comprising administering thalidomide in combination with prednisone as recited in the '847 application claims anticipates the claimed method of treating "blood-born tumors" comprising administering thalidomide". The "comprising" language of the instant claims allows for the administration of other active agents such as prednisone as recited in the claims of the '847 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

March 2, 2010